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THE ORIGIN AND NATURE OF THE HYPOGLYCEMIC THERAPY OF THE PSYCHOSES*

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Three and one-half years have now passed since I first reported a new method of treating psychoses to the Medical Society of Vienna. The treatment was new because it was the first to make use of the hypoglycemic state for therapeutic purposes. Hypoglycemia was up to then universally avoided because it was dangerous; this was the first time that a method was developed which at once diminished its danger and utilized its effects.

Three and one-half years have passed and I am now in a much better position to report not only my own experiences but also the corroborations of the work which have since appeared in many countries, so that my own original observations can now be said to have been tested and confirmed. That this has been possible is due to the tireless efforts of a man to whom my deepest thanks are due; a man who has not only lent his scientific authority but also the entire strength of his character unselfishly to the promotion of this work. The man to whom I refer is the head of the Psychiatric University Clinic of Vienna, Professor Otto Poetzl. My thanks are due to him not only for personal reasons but for impersonal reasons also. If he had not extended his help and placed his clinic at the disposal of this work, it might have taken a long time or might even have been impossible to develop this new therapy.

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The idea of hypoglycemic and hypoglycemic shock treatment of psychoses goes back to the year 1928, although it required time thereafter to develop the therapy to the point where it could be practised in the way I described in my monograph. The idea behind this treatment was a logical consequence of the idea which led me to introduce moderate doses of insulin in the treatment of morphine addiction. The observations I made in connection with a few instances of accidental deep hypoglycemia in the course of this treatment of drug addiction, encouraged me to attempt the use of hypoglycemia in the treatment of psychoses; for the changes I saw in the mental picture both during and after deep hypoglycemia were remarkable and demonstrated to me beyond a doubt that hypoglycemia either directly or indirectly can influence psychotic states in a way that could be put to practical use.

It was at this point that I made the transition from insulin treatment to hypoglycemic treatment of psychoses. But before all these considerations could be developed into a practically useful form of treatment, a method had to be developed by means of which we could reduce the possible dangers, which were certainly overestimated at that time, to a minimum. A technic had to be found which would permit us to recognize dangers as they occurred so that we could avoid them or prevent them. Definite procedures had to be found for meeting each of the complications as they occurred.

When this method was developed we could say that we could now utilize hypoglycemia as such in the treatment of psychoses without running any great risk. But this method in itself did not tell us how it could be applied so as to achieve the best therapeutic results. In fact in most cases it was only when we approached the danger zone that we could achieve the best therapeutic results. If instructions are followed carefully and a standard technic is used the treatment is relatively safe but it is nevertheless true that it is possible to avoid all the attendant dangers and at the same time forget that the real purpose of the treatment is to cure the psychosis. If one is too preoc-

cupied with the possible dangers of the treatment, he is in danger of forgetting its actual purpose. Success depends on the right combination of both considerations. I shall now briefly sketch the procedure without going into the theoretical considerations which underly it, for the time at my disposal is not only short but the theories themselves are rather vague and of no great practical significance.

The method which I have described in my monograph is only meant to be an outline which has to be modified in each individual case. Therapeutic results depend not only on the production of a hypoglycemic state but on the proper use and management of every single hypoglycemic shock. The results do not depend on the size of the dose of insulin but rather on the proper termination at the right time of each hypoglycemic state. One has to be acquainted with the various conditions that arise and needs considerable personal experience before he can manage the hypoglycemia effectively. It may also be emphasized that one has to be a good psychiatrist in the ordinary sense with sound psychological judgment and insight. Psychological considerations are important throughout the treatment. Without doubt we now believe that in mental disease as in physical, psychological factors are not only of psychological consequence but may produce also pathophysiological changes through the vegetative nerves and indirectly may even produce anatomical changes. If this be true how can anyone believe that psychological factors and psychological attitudes are unimportant considerations?

When the treatment first developed I could not say exactly why I would terminate the hypoglycemia at one point in one instance and at a different point in another, or why I would vary the period of hypoglycemia in the same patient in different stages of treatment. The probability is that I was guided by dim subconscious recollection of my prior experiences in similar instances. It was only after a time that I was enabled through retrospection to indicate in a general way certain principles of management for different groups of patients and I hope that in

spite of the difficulties involved in the treatment, these guiding principles will permit a wider application of the method. It should not be forgotten that this treatment is not merely pharmacological. It would be more appropriate to say that the medicine is used as a tool and as in any other treatment which depends on the use of instruments, one must first learn how to handle the tool, then seek to improve the technic. It is emphasized that a superficial knowledge of the simple principles of the method does not suffice. Before the therapeutic possibilities of hypoglycemia can be explored, the technic has to be learned just as the technic for a surgical operation.

THE METHOD

This consists of four phases:

Phase 1. Preparatory phase
Phase 2. Shock phase
Phase 3. Rest period
Phase 4. Polarization or terminal phase

PHASE 1: The initial dose varies from eight to thirty units of insulin depending on the patient's physical condition and the duration of his illness. The injection is given in the early morning to the fasting patient and four hours later he is given a solution of glucose. The dose is increased five or ten units daily until the patient begins to show his first hypoglycemic symptoms three or four hours after the injection. As soon as hypoglycemic coma is obtained, Phase 2 begins.

PHASE 2: After the proper dose has been reached the patient is given a shock dose daily. This shock dose, however, does not necessarily remain constant. Very often in the course of treatment the patient may develop coma with a much smaller dose. It rarely happens that the shock dose has to be increased after it is found. Coma is terminated four or five hours after the insulin injection with a nasal tube feeding of 400 c.c. of sugar solution containing 100 to 200 grams of sugar, depending on the amount of insulin that is given.

The most important point in the treatment is to know when to terminate the hypoglycemia. In deciding when to terminate we are guided by two considerations which unfortunately do not always coincide. The first consideration is the patient's physical condition, with particular consideration to danger of collapse. When there are danger signs, we must end the hypoglycemic state whether or not we think it is advisable from the viewpoint of the patient's mental condition. The only other consideration in deciding when to terminate is whether or not it will benefit the patient's mental state.

Whenever a dangerous or threatening situation arises, the hypoglycemia is quickly terminated with intravenous glucose administration or with adrenalin. Phase 2 is continued until the desired results are achieved.

PHASE 3: This phase is no longer considered important. It is a day or more of rest and only becomes necessary because the patient grows physically exhausted from shock or repeated hypoglycemia.

PHASE 4: During the terminal phase which lasts from four to eight days, the patient is only given a small dose of insulin as compared with his shock dose and the hypoglycemia is terminated in two hours with the administration of glucose.

I realize that even though I have given you only a brief description of the hypoglycemic method of treatment, I have told you nothing of the value or effectiveness of the treatment. Since I know that this interests you most, I shall try in the short time at my disposal to describe briefly some typical reactions of psychotic subjects to hypoglycemia.

THE INFLUENCE OF HYPOGLYCEMIA ON HALLUCINATIONS

The mental changes that occur in a psychotic subject in the course of treatment are usually so surprising and dramatic that it is difficult to describe them accurately. With few exceptions all sorts of hallucinations—visual, auditory and somatic—are diminished or disappear totally during hypoglycemia, at first only for a short time and

during a certain stage of the hypoglycemia. A patient, for example, with paranoid ideas or with ideas of reference suddenly loses his hallucinations when the hypoglycemia has reached a certain depth and may suddenly for a short time show an insight into the hallucinations which he has just had.

At the beginning of treatment the patient regularly becomes psychotic again as soon as the hypoglycemia is ended. One gets the impression that the patient has two kinds of consciousness and that he has exchanged one for the other. When one has seen this dramatic change he begins to appreciate why people in the olden days spoke of a man's being "possessed".

As treatment progresses the lucid phases during hypoglycemia become more and more protracted and finally begin to survive the point of termination. The patient then remains clear and free of his hallucinations for a considerable time. Cases which are progressing favorably remain symptom-free throughout the day until the following treatment next day; that is, they remain without hallucinations and show insight into their illness. At this point a curious thing happens: The same patient who at the beginning of treatment had lucid periods during hypoglycemia only to become psychotic again after termination, now for the first time becomes completely symptom-free throughout the day but begins to show psychotic symptoms again for a short time during hypoglycemia. In other words he now shows a reversal of reaction. In effect then, the hypoglycemia at first revives the normal personality of an acutely psychotic individual. Later when the patient has improved, the hypoglycemia serves to revive the psychosis which had been repressed but not yet eliminated. However, these psychotic symptoms of hypoglycemia are themselves soon diminished and finally eliminated, so that the patient is at last symptom-free both during hypoglycemia and thereafter.

In other cases the hypoglycemia, instead of provoking a lucid phase, converts the patient's mental picture into something that is just its opposite. A stupor for example,

may be converted into a productive psychosis or the patient awakens in normal mental state. As the patient improves and remains awake, even outside of hypoglycemia, he may in the final stage of treatment again become stuporous for a short time during hypoglycemia, so that there is again a reversal of reaction. Not only the patient's mental picture, but the patient's emotional state as well may be converted into its opposite under the influence of hypoglycemia. After one has had considerable experience one gets the impression that every hypoglycemic state removes another portion of the psychosis and allows another bit more of the repressed normal personality to achieve dominance. What we attempt to do in the course of treatment is to stabilize or fixate the dominance of the normal personality.

If we sum up this superficial description of the patient's reaction to hypoglycemia, we get the following impression: The hypoglycemic state weakens, inhibits and finally represses that portion of the mind which happens to be most active at the time, so that the hitherto latent subdued and repressed portions—if I may so express myself—are again brought to the surface so that they can again prevail over the elements which are now repressed. This is particularly clear when the hypoglycemia reaches its greatest intensity just before the onset of coma.

In cases which run a favorable course, the repeated hypoglycemic states finally eliminate the psychosis so that the normal personality can again achieve complete dominance. By way of illustration, I shall describe one of many cases: A 20 year old girl is admitted for treatment. Her illness dates back about a year and a half before her admission. For the past eleven months the patient had been given all the modern forms of treatment, such as malaria, typhoid vaccine, endocrine treatment, sleep treatment. The psychosis developed further and the patient's condition was getting worse. She was diagnosed as a hebephrenic schizophrenia, and the consultants said at first that the outlook was dubious and later declared that her condition looked more and more hopeless. Some of

the best known psychiatrists in Europe had been interested in the case.

On admission the patient was mute and had to be tube fed. She lay continuously in a stereotyped embryonic position, kept grimacing and appeared very apprehensive. For months the patient had remained in this condition, completely indifferent to her personal needs and only occasionally showed transitory periods of excitement. I shall only try to give you a brief sketch of the course of her treatment. After the first insulin injection of 30 units the patient's attitude grew somewhat more relaxed and three hours after the injection the patient got out of bed, asked for food, and occasionally responded to questions. On the following days the patient's reaction was less marked and she apparently showed little response except with regard to her habitual position. Every time the patient passed into a hypoglycemic state, she abandoned her embryonic position and lay in a normal position in bed. She did not show the least degree of somnolence and seemed to be unchanged otherwise. The patient had not yet gone into coma but she again returned to her former stereotyped position from which it was impossible to move her.

As the dose was further increased the only change was that she grimaced less frequently. The patient had her first comatose reaction in the third week of treatment after an injection of sixty units of insulin. At this time the patient was still negativistic, apathetic, stereotyped and inaccessible. Three and one-half hours after the injection of sixty units of insulin, the patient became comatose. When she awakened, she acted like a person who had just been in a deep sleep. "Where am I?" she asked, "What day is this?" As she spoke she gradually grew more composed and began to realize where she was. The patient spoke of her hallucinations with full insight. "I thought I was in a hotel where I was being kept as a prisoner. I thought the doctors were waiters who had been bribed to keep me here. I heard other prisoners in the next room calling out for help." She said she struck her parents because

she thought they were behind all this. The patient gradually began to show a normal emotional response. She began to cry. She said she was afraid that her parents might blame her for her behavior. They might not realize that she was very sick and might hold it all against her. After a few hours had passed, this phase of lucidity began to disappear, but the patient continued to be talkative throughout the day. The following day, after the hypoglycemia was terminated, the patient took a walk in the garden with her mother, and was able to converse fairly well. The patient, however, was still having hallucinations. She suddenly snatched up some fallen leaves in the garden and said that they were made of gold. On the third day, as the patient awakened from hypoglycemia, she said spontaneously, "I had some funny ideas yesterday. I thought there was gold lying around in the garden, that somebody had left it there for me." After each successive hypoglycemic period, the patient progressed another step forward. After eight days had passed, the patient was completely symptom free, with full insight into her illness. When some books were offered to her, she looked them through, and said she thought they would make heavy reading for a person in her condition, but she refused to talk about her past behavior. She went to the movies, and acted in a perfectly normal way. Treatment was continued, however, until the patient no longer showed the least trace of her previous psychosis.

Three and a half years have since passed, and the patient continued her former studies as a University student, and is in complete health.

However, not every case has so short or even a course. But the following case will again show how close the relation must be between the treatment and the improvement. The patient was a woman of fifty years whose history indicated the presence of a long-standing but relatively mild paranoia which must have existed for a decade, although the patient had always adjusted fairly well. She was married and had children, one of whom was schizophrenic.

The paranoid condition continued throughout the patient's married life although she could conceal it very successfully. It was discovered that the patient, who was a woman of means, would occasionally hire female detectives to act as domestic servants to protect her from the threats of her enemies. When the patient was fifty-four years of age she suddenly grew worse and had to be confined in a hospital. She grew dangerously aggressive and made two attempts at suicide. She also developed auditory and visual hallucinations and became very disturbed. After the patient had spent two years in a private sanitarium, her husband managed to have her stay in a secluded villa with two physicians and attending nurses. Professor Willmarr, who was interested in the case, told the husband that the prognosis was most unfavorable and that there was no hope of improvement. At Willmarr's suggestion it was decided to try hypoglycemic treatment as a last chance. After four weeks of treatment, the patient showed improvement in spite of the fact that the patient's condition was complicated by diabetes and other disabilities. After the patient was under treatment for four weeks, I was called. In eight days during which the patient was successfully brought into deep shock, she had become perfectly clear and begun to show some insight into her illness. In two weeks she was sufficiently improved to take a trip to Italy with her husband. She now writes that she is in excellent condition, and her husband states that it has been ten years since she has been so well.

I have only selected two cases from a great many to indicate that there is a close connection between the treatment and the patient's improvement. From a large and varied number, I have chosen a few interesting and typical examples of the influence of hypoglycemia upon psychotic states. It is not merely my own impression that prompts me to say that anyone who has sufficient experience with the treatment and some insight into the phenomena must recognize that hypoglycemia has a special influence on a psychosis. One cannot escape the impression that he may deliberately influence the nucleus of the psychosis by

hypoglycemia. Quite aside from the therapeutic results, the entire phenomena and the individual reactions are sufficient to show that the psychosis is influenced in a special way by hypoglycemia.

Improvement, it is true, may just happen to coincide with the treatment, but when such coincidences occur so often, it must be assumed that they are more than merely accidental.

My own experience now includes over 300 cases, and there are as many more cases treated under my supervision by others, but I am perfectly well aware of the difficulty there must be in reducing the material to statistics from which the value of a new treatment of schizophrenia can be determined. The natural fluctuation which occurs in the course of the disease, the absence of the definite symptoms that we have in physical diseases, and the impossibility of making a certain prognosis in a particular instance, all make it difficult to estimate results, especially when the number of patients observed is small. When in so large a series of patients as I have treated up to now, and with the results confirmed by others, the net result is a percentage of remissions which is at least four times greater than the most optimistic figures for spontaneous remissions, then I think, the most conservative will conclude that this treatment is effective.

In estimating the results of this treatment, one has to distinguish between recent cases, that is cases of no longer than six months duration; chronic cases, that is cases of over a year and a half duration; and the group of cases between six months and a year and a half duration. In formulating this estimate I attach particular importance to the definite concept of a full remission. A full remission means that the patient is symptom-free after the treatment has been concluded, that he has full insight into his illness, that his emotional reactions are normal, and that he can return to his former work. In addition to full remissions, I speak of good remissions—that is, a condition in which the patient is free of schizophrenic symptoms, and can re-

sume his former work, but has some slight degree of defect. And finally, I speak of social remissions. The concept of mere improvement has not been used in formulating the statistical results. After defining these concepts and reviewing my first group of over 100 cases carefully, I have found the following results: In recent cases, 88 per cent had good or full remissions, and could go back to their former work. Of these, 70 per cent were full remissions. In all other cases, that is all cases of over six months duration, the results vary in direct relation to the duration of the illness. Forty-seven per cent of the cases showed good remissions with capacity to work, of which 19 per cent were full remissions.

When we examine the statistics for spontaneous remission in schizophrenia in various countries, we find that the figures vary between 5 and 20 per cent of remission, according to the author. Even if we compare it with the optimistic figure of 30 per cent, we still have a large balance in favor of the treatment. I should like to add that I formerly thought that only recent cases would show a satisfactory response to treatment. Later I realized that in some chronic cases more or less improvement was possible, and it was well worth trial, for it is not a matter of indifference if the chronic cases can be improved. When one considers how serious a problem chronic schizophrenia has become, and how much can be done to improve these conditions, it seems well worth the effort.

At the invitation of State Commissioner Dr. Parsons, I have recently conducted a course in the technic of this treatment for twenty-five physicians, representing the various New York State Hospitals, at the Harlem Valley State Hospital. The case material brought together for treatment in the course of this instruction consisted largely of chronic cases of an average duration of four years. Two cases, at most, were possibly of less than a year and a half duration. The others were some of them mute and apathetic, others disturbed and under restraint, and still others only able to make stereotype movements. Even

with material of this sort, and in spite of the fact that they have up to now had only twenty-five days of treatment, eight patients are already fit for discharge, not as full remissions, but as social remissions who could, under favorable circumstances, return to work. An additional four cases will probably soon become eligible too, so that it can be said that although the treatment has produced in these cases no cures, it has at least proved its value. All the remaining cases with two exceptions, have improved enough to be able to adjust themselves at least to the requirements of institutional life.

Annual Postgraduate Institute

of the

Philadelphia County Medical Society

The New York Academy of Medicine extends its greetings to the Philadelphia County Medical Society on the occasion of the Second Annual Post Graduate Institute, which will be held at The Bellevue-Stratford Hotel, Philadelphia, Pa., April 12 to 16.